

medical care rendered to all patients in the hospital, was found to gain the confidence of the medical staff and did not encounter resistance or resentment. In order to steer clear of the accusation that they were a form of "secret police" or, further, that they trespassed on the doctor-patient relationship, the committee operated strictly as a fact-finding body and played no disciplinary role; included a broad representation of the medical staff with rotation of the representatives; kept meetings open to any member of the medical staff; and identified individual doctors only by code numbers whose names were unknown to the members of the committee.

The role of the pathologist is that of supplier of data. He does not generally participate in the discussion of purely clinical problems, and never assumes chairmanship of the committee.

How then can the audit committee be effective? Because its very existence encourages members of the staff to be thorough and accurate. Questions of policy or discipline are referred to the medical advisory committee; questions of clinical management are referred to the head of the clinical department concerned.

The audit committee described concerned itself first with tissue evaluation and developed a code for the orderly classification of all surgical operations. After this, it ventured successfully into the more difficult area of medical audit, beginning first with a code for the evaluation of deaths, and then studying miscellaneous subjects—duration of tonsillectomies, incidence and prevalence of infections, length of hospital stay, management of duodenal ulcer.

The second participant, the medical record librarian, has the task of securing, preserving and using medical records—the foundation for an effective audit. The quantitative and qualitative requirements for medical records followed standards set by the Canadian Council on Hospital Accreditation. The records must contain sufficient recorded evidence to justify the diagnosis and warrant the treatment and end results.

The librarian also compiles the regular statistics such as the average length of stay per service or the incidence of infections.

An adequate surgical classification code and a code for the evaluation of death are presented. Medical audit check sheets (based on the check sheet of the American College of Surgeons and the Commission on Professional and Hospital Activities, Inc., Ann Arbor, Michigan) enable the auditor to grade the general management of the case stated as excellent, adequate, fair or poor.

Finally, the administrator has the difficult task of creating and maintaining an environment of co-operation to the end of achievement of hospital objectives. The science of administration requires that he be able to "produce the facts" concerning the fundamentals of hospital organization, policy and rules, accreditation standards and principles, and budgetary control. This must be intertwined with and complemented by the art of administration wherein the administrator must try to understand the medical profession, its role in changing society, and social trends, and to dispel any fears that the assumption of a medical audit program will lead to "lay domination".

It is felt by the hospital described that within two years the tissue and medical audit committee had achieved that very delicate balance between respect for the inviolability of the doctor-patient relationship and the hospital's responsibility for rendering medical care of a high standard to the community.

REFERENCES

1. GARWOOD, H. F.: *Hospital Administration and Construction*, 1: 8, 1959.
2. JELAFFKE, M. A.: *Ibid.*, 1: 9, 1959.
3. FOSTER, A. D.: *Ibid.*, 1: 12, 1959.

SERUM VITAMIN B₁₂ CONTENT AS AN INDEX OF HEPATIC DAMAGE

Experimental hepatic necrosis in rabbits was used by Kato and Murakami¹ in Nagoya (Japan) to study the mechanism of an increase of serum vitamin B₁₂ levels. By their method of injecting a single dose of CCl₄, severe histological damage of the liver was produced which, however, was only temporary and recovery without permanent histopathological change was the rule. As a result of this injection, there was marked elevation in the serum vitamin B₁₂ level which paralleled the development of acute hepatic necrosis, and a marked decrease in vitamin B₁₂ storage in the liver. The increase in total serum vitamin B₁₂ within 48 hours after administration of CCl₄ had a quantitative relationship to the decrease in vitamin B₁₂ in the whole liver; this suggests strongly that the rise in serum vitamin B₁₂ level is due to release of stored vitamin B₁₂ following hepatocellular disintegration. Kato and Murakami determined the B₁₂ level by paper electrophoresis and found that the bound vitamin B₁₂ is mainly in the alpha globulin fraction whilst the free form is recovered mainly from the beta globulin fraction. In normal rabbit liver cells, more than half of the vitamin B₁₂ is present in the mitochondria but in the damaged liver its content in the mitochondria is markedly decreased.

This and similar reports throw some doubt upon statements indicating that vitamin B₁₂ protects rats from liver damage by CCl₄ intoxication, but they point to the possible value of vitamin B₁₂ estimation in the diagnosis of liver disease. Rachmilewitz *et al.*² of Jerusalem have continued their investigations into this aspect of vitamin B₁₂ determination in cases of severe congestive heart failure associated with hepatomegaly. They use a mutant of *Escherichia coli* to determine B₁₂ microbiologically and report their findings in 28 patients. Whereas the serum B₁₂ level in normal persons falls within the range of 200 micromicrograms to 500 micromicrograms per ml., these values in most patients ranged from 500 micromicrograms to 3500 micromicrograms per ml. In 11 patients the values were over 1000 micromicrograms per ml., and of five who had normal levels three had congestive failure of recent onset. It is of interest that in one patient whose vitamin B₁₂ level in the serum shortly after admission to hospital was 3500 micromicrograms per ml., it fell to 920 after effective diuresis and decrease in the size of the liver. As against the temporary increase in serum vitamin

B₁₂ in acute liver damage of viral or chemical origin, heart failure with liver congestion causes continuation of a high level as in cases of malignant hepatic metastasis. Rachmilewitz *et al.* suggest the use of vitamin B₁₂ determination as an index of the degree of hepatic damage which is more sensitive than commonly used liver function tests, including serum transaminase estimations. W. GROBIN

REFERENCES

1. KATO, N. AND MURAKAMI, S.: *J. Lab. & Clin. Med.*, 54: 365, 1959.
2. RACHMILEWITZ, M. *et al.*: *A.M.A. Arch. Int. Med.*, 104: 406, 1959.

THE SILENT SCOTSMAN*

When Lady Fleming asked André Maurois to write the official biography of her husband, the discoverer of penicillin, she did a public service and also a special service to medicine. Too often dreary, eulogistic, or simply overly long biographies of the great prevent us from learning by their experiences. Maurois, who started his career as a writer with that brilliant war book "The Silence of Colonel Bramble", is the happiest choice, a Frenchman who knows English and Scots from long, loving acquaintance and skilled observation. He is a practised historian and literary craftsman of the first order. But even these qualifications will not make a great biography unless its subject is worth writing about.

Many have supposed that Sir Alexander was one of those men of modest genius who stubbed his toe on a great discovery, who had greatness thrust upon him by the exertions of others. But Maurois will convince them that they are mistaken. Fleming was something very different, a modest man of genius. It seems that he himself derived a good deal of fun from the "Fleming myth" as he called it, and so he may have been responsible himself for a story told about him in the early 1950's. Apparently during one of the conferences regarding the development of penicillin in Britain, an argument developed and a small man got up and protested, "But after all it is my baby!" A voice at the back echoed, "And you left it out on Florey's doorstep and you should have been shot for it!" Maurois shows clearly that Fleming did no such thing. He understood perfectly the implications of the vagrant mould which had blown on to his culture plate in the little, cluttered laboratory in Paddington. He communicated his findings to learned societies with great clarity. He told his colleagues repeatedly that penicillin was much better than sulfonamides, which were the wonder drugs of the late 1930's. But somehow he could not get them to listen, or if they did listen, to take what he said seriously. Sir Henry Dale is very frank and helpful about this and he says, "I very well remember his interesting paper and the way in which we all of us said 'Charming, wasn't it?' Just the sort of naturalist's observation Fleming would make and that was all." And again

another time, "Oh yes, we said. Fleming does observe that nice sort of thing"—He was very shy and excessively modest in his presentation, he gave it in a half-hearted sort of way, shrugging his shoulders as though he was deprecating the importance of what he said. At the same time the elegance and beauty of his observations made a great impression. It is possible that Sir Henry has seen the matter with a certain rosy retrospection, for no one asked any questions and the unlucky Fleming must have felt that he had cast his pearls before swine who had not even noticed them or him.

He made strenuous efforts to isolate the entire principle from *Penicillium notatum* on his own and constantly encouraged others to do so. But he had very small resources and was not very adroit at obtaining money, and his chief, the massive dogmatic Sir Almroth Wright, a great immunologist, did not believe in chemotherapy. Furthermore, the chemistry of penicillin proved to be difficult. Indeed, when Florey and Chain eventually solved the problem more than a decade later new chemical methods played a part. This does not in any way reduce Florey's wisdom in reopening the matter, Chain's great skill and the timeliness of the Rockefeller Foundation grant which allowed them to do the work.

Maurois has not explained Fleming's failure to get support as fully as one would have liked. He was respected, even admired, but for some mysterious reason not taken seriously, in spite of being a man whose ability was fully recognized by his peers. The mystery is important, for one wonders how often Flemings are neglected in this way.

Perhaps we can learn something by contrasting him with Sir Frederick Banting who was his junior by 10 years and who died about 14 years before him—50 years of their lives overlap. Banting made his great discovery in his early thirties and for the 20 years which remained to him he was honoured. He was one of the great amateurs. Fleming was the professional *par excellence*. Trained by and perhaps too long in the shadow of Almroth Wright, Fleming would have had a great scientific reputation had he died in 1929 when he made his discovery. He was not an amateur. He was an extremely competent technician and a master of improvisation. He had introduced Paul Ehrlich's Salvarsan, 606, the magic bullet, to Britain. He was one of those strange, reticent, visionary Scotsmen who had learned how to keep one eye peering down a microscope and the other on some improbably distant horizon. Such men have always been a puzzle to Englishmen. Looked at one way, Fleming was a dry, commonsense, prosaic, almost pawky Scot—yet inside was lurking someone very different but nearly inarticulate. Sometimes that romantic watcher from the wings almost broke loose, and the discovery of penicillin was one of those rare occasions. Luckily it happened once again towards the end of his life when he made a second marriage, to a Greek lady. It was she who had the good sense and fine taste to place his papers in the hands of André Maurois. This is perhaps *the* biography of a professional medical researcher. Fleming, whether he recognized it or not, is clearly what C. P. Snow would call one of "the new men", a moulder of our

*The Life of Sir Alexander Fleming, by André Maurois. Translated from the French by Gerard Hopkins. 293 pp. Illust. Jonathan Cape, London; Clarke, Irwin & Company Limited, Toronto, 1959. \$5.50.